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| EXAMINER | |
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| SWITZER, JULIET CAROLINE | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/800,322 | JAMES ET AL. | |
| | Examiner | Art Unit | |
| | Juliet C. Switzer | 1634 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-8,13 and 16-83* is/are pending in the application.

4a) Of the above claim(s) *2-4,6-8,17-31 and 34-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,13,16,32,33 and 83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/29/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. Currently, claims 1-8, 13, 16-83 are pending. Claims 1, 5, 13, 16, 32, 33, and 83 are under prosecution. All other claims are with drawn as being drawn to non-elected inventions.

2. Claim 16 is being considered only insofar as the second nucleic acid molecule is (ii), "a nucleic acid molecule comprising a nucleotide sequence capable of hybridizing to the complement of SEQ ID NO: 7…under high stringency conditions." All other possible molecules recited as the second molecule are withdrawn from prosecution as being part of non-elected combinations.

3. **This action is final.**

4. Applicant's IDS submitted 4/29/08 has been considered. It is noted that Mack et al. (US 2003/0235820) teach that KIAA1199 protein is upregulated in colon cancer derived liver metastases compared to normal colon tissue. Although applicant states that instant SEQ ID NO: 7 "corresponds to KIAA1199" the examiner was not able to establish a relationship between instant SEQ ID NO: 7 and the sequence referred to by Mack et al. (AB033025, GenBank record). For at least this reason, no art rejections are set forth in view of the submitted references.

### *Claim Objections*

5. Claims 16, 32, 33, and 83 are objected to because they recited non-elected subject matter in the alternative.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 5, 13, 32, 33, and 83 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention and breadth of claims

7. Claims 1, 5, 13, 32, 33, and 83 broadly encompass a method of determining the onset or a predisposition to the onset of a gastrointestinal tract neoplasm in an individual said method comprising measuring the level of expression of SEQ ID NO: 7 or a related nucleotide sequence capable of hybridizing to SEQ ID NO: 7 under "high stringency conditions." The claims set forth that an increase of said nucleic acid molecule relative to the normal level of expression in an individual is indicative of the onset or predisposition to the onset of said neoplasm. It is noted that applicant amended claim 1 to delete the language "or a predisposition to the onset" but did not delete the corresponding language from the end of the claim. Therefore, the claims are

considered to still encompass methods directed towards determining a predisposition to the onset of colorectal adenoma.

The invention is in a class of invention which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed. Cir. 2001).

"Measuring the level of expression" is understood in light of the specification to be a measurement of transcription or translation of a nucleic acid molecule- that is measuring mRNA products or measuring expressed protein products (p. 23 of specification).

"A nucleotide sequence capable of hybridizing" to SEQ ID NO:7 "under high stringency conditions," encompasses many nucleic acids that would hybridize to SEQ ID NO:7 or its homolog or a variant or a homologue or a splice variant of SEQ ID NO: 7.

"Biological sample" is a broad term that includes any sample of biological material including urine, hair, prostate, breast, as well as blood, serum, saline solution extracted from the lung following lung lavage or the solution retrieved from an enema wash. Claim 33 recites that the sample is a biopsy sample, but does not limit the origin of the biopsy- thus still encompassing biopsy of tumors of any origin. However, the specification does not teach overexpression of SEQ ID NO:7 functional derivatives, any variants or homologs of SEQ ID NO:7 in any other tissue except colorectal tissue obtained from colonoscopy. The specification teaches the sequence is from a human colorectal biopsy sample (page 97, line 4) but does not teach any other source in human and any source of sampling in other non-human individuals that this sequence is overexpressed in other neoplasms.

The specification only teaches overexpression of the SEQ ID NO: 7 sequence in colorectal adenoma which is a benign tumor of epithelial origin which is derived from glandular tissue (p. 1 of specification). The specification teaches the adenoma biopsy samples from human patients with adenomas undergoing colonoscopy. The specification does not teach any other source of tissue samples that could be used to determine the onset or predisposition to the onset of colorectal adenoma. Many transcripts are tissue- and tumor-specifically expressed at different levels. For example CD44v expression level is high in all metastatic brain tumors but virtually negative in tumors metastatic to the spine (Resnick et al., 1999, Molecular Diagnosis, 4: 219-232).

Each of the dependent claims recites a further limitation, for example, wherein the nucleotide sequence is SEQ ID NO: 7, wherein the subject of detection is the expression product of said nucleic acid sequence, wherein the neoplasm is colorectal neoplasm, or in particular adenoma, and wherein the adenoma is a tubular adenoma, tubulovillous adenoma, or a villous adenoma, but all of these claims still encompass breadth and subject matter which is problematic and discussed in this office action.

Guidance in the Specification and Working Examples

The examples in the specification teach differential display analysis of samples of adenoma and normal tissue obtained from patients undergoing colonoscopy, comparison of the isolated sequences to nucleic acid databases housed by NCBI using BLAST, and RT-PCR confirmation of the differential expression of the isolated molecules (examples 1-3). Example 4 describes the testing of 71 colon adenoma tissue samples by quantitative RT-PCR and comparison of the expression levels to the mean expression levels of normal tissues. From these results a "fold increase" was tabulated for each isolated nucleic acid. The specification teaches

on page 79, Table 2 that SEQ ID NO: 7 corresponds to Adenoma Marker clones named 12-2f and 8-2d. The specification does not teach how SEQ ID NO: 7 is related to the inserts from these clones nor does the specification disclose how the inserts in the clones are related to one another.

Table 3 from the specification teaches that clone 8-2d was, on average, upregulated 50 fold relative to the mean expression levels of normal tissues, and that clone 12-2f was on average, upregulated 45 fold relative to the mean expression levels of normal tissues (table 3), and that both clones were upregulated greater than 5-fold in 100% of the adenoma tissues (table 5). The specification also teaches, however, that 19% of the normal tissue samples showed upregulation of both of these clones (table 6 and table 7).

The specification repeatedly refers to clones 8-2d and 12-2f as being different clones, with these two clones presenting with different results in Table 1 and as part of different groups of diagnostic markers in Tables 9-15, but the specification is silent as to how the two clones are actually related, or what the sequence of the insert of the individual clones are or how these clones relate to SEQ ID NO: 7.

There is no external working example which validates the use of SEQ ID NO: 7 as a marker for colorectal adenoma.

The data given in the tables is given as averages- the mean fold increase in adenoma samples versus the mean expression level of normal tissues. For both normal and adenoma means, no mention is given in the specification as to the ranges of observed values, the variation among samples or any formal statistical analysis to determine if the differences observed between types can be attributed to sample effects of to the chance of error. This is a significant absence given that the specification teaches that 19% of normal tissues also over expresses both clones.

The specification does not provide any evidence that an increased expression of SEQ ID NO: 7 related sequences (that is sequences which hybridize under "high stringency" to SEQ ID NO: 7 but are not 100% identical to SEQ ID NO: 7) can be used as a marker for the presence of colorectal adenoma in colon tissue samples.

The specification exemplifies that clones 8-2d and 12-2f have levels of expression higher than five fold versus average expression in normal control tissue in 100% of adenoma tissues, but the specification does not demonstrate that high levels of expression could be observed in other types of tissues- blood or urine or stomach tissues- or even that if it were that it would indicate colorectal adenoma. However, the specification does not teach any other examples in any other tissue, neoplasm or nucleic acids comprising of SEQ ID NO: 7 sequences with deletions, additions, substitutions and variants, homologues, functional derivatives or guidance as to what sequences or features of SEQ ID NO: 7 sequences or its variants, homologues, functional derivatives sequences would hybridizes to SEQ ID NO: 7 and would meet all the limitations of the instant broad claims where such a nucleic acid can be used to determine the onset or a predisposition to the onset colorectal adenoma in any human by measuring elevated expression levels of the sequence.

Further, the claims are drawn to encompass determining a predisposition to the onset of gastrointestinal tract neoplasm. The specification, however, only demonstrates overexpression of the subject clones in actual colorectal adenomas. The specification does not demonstrate that expression of these clones increases prior to the presence of the adenomas in the colon or rectum.

The specification does not demonstrate the detection of SEQ ID NO: 7 translation products, nor does it demonstrate that these putative translation products are detectable at different levels that could be used as set forth in the claimed methods.

The guidance provided by the specification amounts to an invitation for the skilled artisan to try and follow the disclosed instructions to make and use the claimed invention.

The unpredictability of the art and the state of the prior art

It is highly unpredictable whether sequences which hybridize to instant SEQ ID NO: 7 under "high stringency" conditions will also be markers for colorectal adenoma. High expression of Prostate specific membrane antigen (PSMA) in more aggressive prostate cancer makes PSMA a potential diagnostic target for prostate cancer (Schmittgen et al., Int. J. Cancer, 2003, 107:323-329). PSMA has three alternatively spliced variants, PSM', PSM-C and PSM-D. When PSMA and the alternatively spliced variant levels were compared by qPCR methods in various samples of normal, benign, primary and metastatic tissues from much larger sample size of 72 patients, however, the results indicate complex and contradictory expression profiles of the splice variants quite different from the initial PSMA expression patterns (Table III). For example although PSMA mRNA levels were seen increased 3-fold in primary prostate tumor, bone and lymph node metastases samples compared to normal prostate it was not increased in liver metastases samples but in fact decreased slightly. Therefore an increased PSMA mRNA expression level may be a marker for prostate tumor, bone and lymph node metastases but not for liver metastases. Additionally, not all PSMA variant transcripts showed increased expression levels in prostate tumor as the splice variants PSM-D expression level is not increased but rather decreased. PSM-D mRNA level, on the other hand, is increased in other types of tissues such as bone and lymph node metastases samples. Therefore the art teaches the use of a marker for disease risk assessment is unpredictable depending on the variants, biological sample and sources, and types of neoplasm.

Because the claims encompass the analysis of translation products of SEQ ID NO: 7 or translation products of nucleic acids that hybridize to SEQ ID NO: 7 under high stringency while

the specification provides only an example of the analysis of mRNA levels by differential display and quantitative RT-PCR, it is relevant to point out the unpredictability as to whether or not a measure of any nucleic acid expression is indicative of the level of protein in a sample. The post-filing art of Chan teaches that cells have elaborate regulatory mechanisms at the level of transcription, post-transcription, and post-translation (p.1, last paragraph), and that transcript and protein abundance measurements may not be concordant (p.3, sixth full paragraph). Thus it is unpredictable as to whether or not the results pertaining to nucleic acid expression, as presented in the instant specification, would be applicable to methods requiring or encompassing the analysis of a protein samples.

Even if the claims were limited to determining the overexpression of SEQ ID NO: 7 in a human patient wherein the sample is a colorectal biopsy, and the claims were amended to recite a method for detecting the presence of colorectal adenoma because the actual data given in the specification is not enough to apprise on of skill in the art with particularity as to how to practice the invention. That is, there no guidance or showing that demonstrates the range of values observed in the adenoma versus normal samples, and the specification teaches that at least 20% of the normal samples overexpressed the subject clones. It is highly unpredictable, therefore, what level of expression of SEQ ID NO: 7 must be observed in order for one to successfully conclude that adenoma is present or more likely than not present. In order to use the claimed invention, in any embodiment, one would have to undertake an extensive amount of unpredictable experimentation.

Quantity of Experimentation

The quantity of experimentation in this area is extremely large since there is significant number of parameters which would have to be studied such as detection of elevated expression of SEQ ID NO: 7 functional derivatives, variants, functional derivatives, homologs and other SEQ ID NO: 7 sequence-related nucleic acid molecules with all types colorectal adenoma in himans that meets the limitations of the instant claims and determine if each sequence expression level increase in all types tissues can be used as a marker for the onset or a predisposition to the onset of any neoplasm in any individual. Furthermore, one would have to discover the expression product or products of SEQ ID NO: 7 and establish reliable methods of detection and that this product is in fact translated in patterns similar to the transcription patterns of the observed mRNA. This would require extensive experimentation and specific guidance, with many intervening steps, upon effective reduction to practice, not providing any guarantee of success in the succeeding steps, which are not routine, and an artisan of skill would not have known at the time of invention.

Level of Skill in the Art

The level of skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, in a highly unpredictable art where an increased expression of a DNA marker is asserted to be associated with colorectal adenoma, the specification provides minimal guidance for a specific example (the expression levels of two clones in colorectal adenoma tissue) and no guidance to support the limitation of the instant claims wherein overexpression of any SEQ ID NO: 7 functional derivatives, variants, functional derivatives, homologs and other SEQ ID NO: 7 sequence-related nucleic acid molecules can be used as a adenoma marker.

Further, the prior art and the specification provides insufficient guidance to overcome the art recognized unpredictability of different expression patterns for splice variants. Therefore the

use of splicing variants are unpredictable as marker sequences. for all types of neoplasms in various tissues and sample sources. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written.

***Claim Rejections - 35 USC § 112-Description***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 5, 13, 32, 33, and 83 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a method of determining the onset or a predisposition to the onset of colorectal adenoma in an individual comprising measurement of the level of expression of a nucleic acid, (a) comprising SEQ ID NO:7; (b) any nucleic acid sequence capable of hybridizing to SEQ ID NO:7 under high stringency conditions. The broad genus encompassed by the claims includes methods which detect SEQ ID NO: 7 as well as SEQ ID

NO: 7 variants, functional derivatives, homologs and other SEQ ID NO: 7 sequence-related nucleic acid molecules.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that Vas- Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In The Regents of the University of California v. Eli Lilly (43. USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B (1), the court states that "An adequate written description of a DNA. . .' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention.

In analyzing whether the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure.

With regard to “a functional derivative, variant or homologue”, the specification does not teach any structure of a DNA sequences that would be a functional derivative, variant or homologue of the human SEQ ID NO:7 or a sequence that hybridizes to SEQ ID NO:7 under a

low stringency conditions, in any individual, nor does it provide any guidance as to the structure of such sequences in any individual. Many alternative splicing variants, for example, encode proteins with vastly different function, localization and expression. Two functionally disparate PSMA and PSM' polypeptides with differential cellular localization are generated from the protein-coding sequences of the same gene. The expression levels of the two functional derivatives from splicing variants of the same gene are different depending on tissue-type and tumor-type as explained above (Schmittgen et al., page 323, right column, paragraph 1). Therefore, sequence variants or homologs may have vastly different functions and expression patterns and levels and therefore may not be used as markers for the same biological functions such as onset or predisposition of neoplasm. In addition, functional derivatives of PSMA alternative transcripts as described above exemplify that functional derivatives have tissue- and tumor-specific expression levels. For example, translation of PSM-C mRNA results in a protein that is identical to PSM' and therefore with identical function; however, the expression levels of the two transcripts are quite different. The expression levels of bone metastases PSM-C is increased approximately 2-fold but the identical transcripts that encode identical proteins is seen decreased in the samples. Therefore even two transcripts that encode identical proteins with identical function can have differential expression patterns depending on tissue and tumor types.

With regard to "a nucleotide sequence capable of hybridizing to any one or more of the sequences" of SEQ ID NO:7 "under high stringency conditions", the specification does not teach any structure of a DNA sequences that would hybridize to SEQ ID NO:7 under the recited high stringency condition in any individual, nor does it provide any guidance as to the structure of

such sequences in any individual. The specification has not discussed any structural features which are essential for such a molecule to be a marker for colorectal adenoma.

Next, it is determined whether other identifying characteristics have been described that will describe other members of the genus. In the instant case none of the identifying characteristics that would identify potential related nucleic acid markers as neoplasm markers have been described other than the primary structure of SEQ ID NO: 7. The specification teaches the sequence SEQ ID NO: 7 but no identifying characteristics that can be used to identify other sequences encompassed by the broad instant claims as colorectal adenoma marker when overexpressed. Therefore, the specification does not teach any relevant identifying characteristics of a representative number of species within the claimed genus to identify a nucleic acid sequence when overexpressed can be used as a colorectal adenoma marker.

Applicant is clearly in possession of SEQ ID NO: 7.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance is what is needed. Since the disclosure fails to describe the common attributes or features of sequences that identify members of the genus, and because the genus is highly variant, and the specification fails to describe other sequences in human than the single species of SEQ ID NO: 7 disclosed and without any guidance to structure/function relationship to determine if a nucleic acid identified would be a useful neoplasm marker, one of skill in the art would conclude that applicant was not in possession of the claimed genus.

**Response to Remarks**

The rejections have been modified to address the amended claims.

Applicant traverses the rejections insofar as they apply to the amended claims.

The traversal has been carefully considered but is not persuasive.

Applicant argues on page 23 that the unpredictability issue raised by the Examiner is not applicable to the presently disclosed and claimed subject matter, pointing out distinctions between the subject matter in this application and the subject matter at issue in Mycogen. However, this misses the point, which was simply to demonstrate that the court has acknowledged that chemistry and the biological sciences are unpredictable arts. In this case, further, the examiner has included a portion of the rejection dedicated to discussion of many of the unpredictable aspects of the claimed invention in view of the teachings in the specification. Applicant states on page 22 that there is no unpredictability regarding whether or nor the expression level of the relevant nucleic acid molecules can be measured, and to a certain extent this is agreed. However, there is a high degree of unpredictability as to how this measurement can be applied to the determination of the onset of colorectal adenoma, as claimed. Further, it is relevant to note that with regard to detecting the polypeptide encoded by SEQ ID NO: 7, there has been no showing of methods which accomplish this end, nor has there been any showing that translation of the polypeptide actually occurs at differential levels in healthy individuals relative to those with colorectal adenoma.

Applicant states on page 27 that the examiner has misinterpreted the invention since Applicants are not claiming a specific percentage above the normal, but, rather, are claiming that any level of expression above normal is indicative of adenoma development. The data in the specification simply do not support this broad statement as the specification shows that about 20% of healthy individuals had expression "above normal." This is part of the point the

examiner is trying to make, based on the teachings of the specification one is merely invited to determine what levels of expression are indicative of colorectal adenoma and what levels are not. There is not sufficient guidance in the specification. While it may be "routine" to determine normal control values as the basis for comparison, in this case it is entirely unpredictable whether those normal control values will be a sufficient marker since some healthy individuals also over-express the clones at issue.

Applicant disagrees that there is no external working example. By this, the examiner means, that applicant has not validated the initial findings in an external sample or actually provided an example where the claimed method was actually used on a human. This is one of the many factors considered when arriving at the conclusion of lack of enablement.

Applicant states that SEQ ID NO: 7 corresponds to KIAA1199 "a molecule known to those skilled in the art." There is no record of any prior art relating to KIAA1199 or GenBank Accession number NC-000015, nor any clear explanation of how these relate to SEQ ID NO: 7, so this argument could not be fully considered. The examiner attempted to "BLAST" the a mRNA sequence which is taught to encode KIAA1199 against SEQ ID NO: 7, and no significant similarity was found (see enclosed BLAST results). Furthermore, it is this argument is spurious and does not address the fact that the specification is silent as to how SEQ ID NO: 7 relates to two different clones, with two different results, which the specification says it is related to.

Applicant states that performing a diagnostic assay, as opposed to differential display is a matter of routine procedure. This does not address the many different aspects of the rejection that have been set forth. As previously noted, the question is not whether one of skill in the art

could analyze expression of SEQ ID NO: 7, but how this relates to determining the onset of colorectal adenoma.

The rejection is maintained.

Regarding the written description rejection applicant submits that nucleic acid claims based on hybridization language may be considered to have met the written description requirement because highly stringent conditions dictate that the species are structurally similar. However, this is not persuasive. Here, there is no description as to which of those "structurally similar" molecules are indicators of colorectal adenoma, as discussed in the rejection.

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the

examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday, Tuesday, or Wednesday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached by calling (571) 272-0735.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Juliet C. Switzer/
Primary Examiner
Art Unit 1634

June 1, 2008